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EXAMINER	
LANDSMAN,R	
ART UNIT	PAPER NUMBER
1647	17

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/431,843	ZAGON ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5,6,14,16,17,38 and 39* is/are pending in the application.

4a) Of the above claim(s) *4 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,6,14,16,17,38 and 39* is/are rejected.

7)☒ Claim(s) *38* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comarison A1* .

DETAILED ACTION

1. Formal Matters

A. Amendment C, filed 5/7/01, has been entered into the record.

B. Claims 1-8 and 14-17 were pending in the application. Claims 2, 7 and 8 have been canceled by the Applicants and new claims 38-39 have been added. Therefore, claims 1, 3-6, 14-17 and 38-39 are pending.

C. All Statutes under 35 USC not found in this Action can be found, cited in full, in a previous Office Action.

2. Election/Restriction

A. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1, 3, 5, 6, 14, 16, 17, 38 and 39, drawn to an isolated nucleic acid molecule comprising SEQ ID NO:1, 4, 5, 7, 9, 11, or 13, vectors, host cells and pharmaceutical compositions, classified in class 435, subclass 69.1.

II. Claims 4 and 15, drawn to an antisense sequence and a pharmaceutical composition, classified in class 536, subclass 23.5.

B. The inventions are distinct, each from each other because of the following reasons:

Inventions I and II are independent and distinct, each from each other, because they are products which possess characteristic differences in structure and function and each has an independent utility that is distinct for each invention which cannot be exchanged.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and recognized divergent subject matter as defined by MPEP § 808.02, the Examiner has *prima facie* shown a serious burden of search (see MPEP § 803). Therefore, an initial requirement of restriction for examination purposes as indicated is proper.

C. A telephone call was made to Frank DiGiglio (#31,346) on July 09, 2001 to request an oral election to the above restriction. Applicant's election of Group I is acknowledged with traverse. Therefore, Group I, claims 1, 3 5, 6, 14, 16, 17, 38 and 39 will be examined, with traverse, in the present application.

Applicant is reminded that upon cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR § 1.48(b) and by the fee required under 37 CFR § 1.17 (h).

Withdrawn Claim Objections

1. Claim Rejections - 35 USC § 112, second paragraph

A. The rejection of claims 1-3, 5 and 8 under 35 USC 112, second paragraph, has been withdrawn in view of Applicants' amendments to the claims in reciting "any one of..."

Maintained Claim Rejections

1. Claim Rejections - 35 USC § 101

A. Claims 1, 3, 5 6, 14, 16 and 17 remain rejected under 35 USC 101 and new claims 38 and 39 are also rejected for the reasons already of record on pages 2-4 of the Office Action dated 1/4/01. Applicants have stated that the proteins encoded for by SEQ ID NO:1 and 5 specifically bind [Met5]-enkephalin and that PGFr antisense molecules increase cell numbers in culture. While the Examiner agrees that the specification does demonstrate that SEQ ID NO:1 binds [Met5]-enkephalin and that the recitation of this SEQ ID NO alone is no longer the basis for the rejection of the claims under 35 USC 101, the Examiner does not agree with Applicants that the specification provides a specific and substantial utility for any of the human sequences, SEQ ID NO:4, 5, 7, 9, 11 and 13. Therefore, the **rejection of claims 1, 3, 5, 6, 14, 16, 17 and new claims 38 and 39 stands** for the previously stated reasons already of record on pages 2-4 of the Office Action of Paper No. 14, mailed 1/04/01, as well as the following reasons.

Applicants argue that SEQ ID NO:5 binds [Met5]-enkephalin (first paragraph of page 5 of Applicants' response dated 5/7/01. However, no binding data could be found in Example 2 or any Examples with regard to SEQ ID NO:5 or any of the other human SEQ ID NOs. Applicants do disclose in the specification that binding studies were performed on human placenta in order to characterize the tissue and that specific, saturable radioligand binding was achieved. However, since this binding was performed on whole tissue, it has not been demonstrated that the radioligand is specifically binding to the receptor of the invention. Applicants also argue that the observation that OGFr antisense molecules increase cell number shows that the sense molecules of the invention encode OGFr. However, the demonstration that the antisense molecules increase cell number does not provide a utility for the OGFr, but only that the antisense is functional.

Therefore, since the nucleic acids do not possess a specific and substantial asserted utility or a well established utility, then the vectors, host cells and the pharmaceutical compositions also do not possess a specific and substantial asserted utility or a well established utility.

2. Claim Rejections - 35 USC § 112, first paragraph - enablement

A. Claims 1, 3, 5 6, 14, 16 and 17 remain rejected under 35 USC 112, first paragraph, and new claims 38 and 39 are also rejected for the reasons already of record on pages 2-4 of the Office Action dated 1/4/01 as well as for the reasons stated in the above rejection under 35 USC 101.

B. Claims 1, 3, 5, 6, 14, 16, 17 remain rejected under 35 USC 112, first paragraph, for the reasons already of record on pages 5-7 of the Office Action dated 1/04/01. Applicants argue that the claimed nucleic acid molecules encode an OGFr, as argued in the above rejection under 35 USC 101. They also argue that the specification teaches how to make fragments of the claimed polynucleotides wherein the protein fragments produced have at least one biological function of an OGFr receptor.

These arguments have been considered, but are not deemed persuasive. First, the argument that these polynucleotides encode human OGFr receptors is not persuasive for the reasons already set forth in the above rejection under 35 USC 101. Since the utility of SEQ ID NO:4, 5, 7, 9, 11 and 13, or the encoded proteins has not been established, then it is not apparent to one of ordinary skill in the art how to use these fragments of a protein with no utility since these fragments would also have no utility. Furthermore, while Applicants have amended claim 1 to recite "at least one biological activity of an OGFr" Applicants have not identified what these activities are. For example, interaction with water molecules could be an activity of the OGF receptors. Therefore, Applicants would not be entitled to the breadth of these claims of "at least one biological activity." Applicants do state that binding to Met-enkephalin or inhibiting cell growth would be activities, but Applicants have stated this *by example only* on page 7 of their response of 5/7/01 and these activities are not part of the claims. Applicants

have not taught the artisan what nucleotides or amino acid residues are critical to perform these functions *in a fragment of the OGFr* encoded for by the claimed polynucleotides.

Applicants have amended claim 3 to recite hybridization conditions. However, an important step in the procedure, the temperature of the wash step, has been omitted from the claim. Applicants would not be entitled to, for example, all nucleic acid molecules which hybridize under the conditions recited in claim 3, but which remain hybridized in a wash temperature of, for example, 40°C since this would be too low. *A high temperature wash step (e.g. 65°C) ,**without adding new matter,** would withdraw the rejection of claim 3 and its dependent claims, 5, 6, 14, 16 and 17 with regard to SEQ ID NO:1 only. However, since SEQ ID NO:4, 5, 7, 9, 11 and 13 have not been shown to have utility, then Applicants have not taught the artisan how to use nucleic acid molecules which hybridize to these sequences.*

Finally, claims 14, 16 and 17 remain rejected under 35 USC 112, first paragraph, for the reasons already of record on page 6 of the Office Action dated 1/4/01. Applicants argue that the specification teaches what diseases to use the claimed pharmaceutical composition for. Applicants state that the amount of nucleic acid to be therapeutically effective can be determined according to age and the condition of the subject and that this determination can be made without undue experimentation. These arguments have been considered, but are not deemed persuasive.

For example, neuroblastomas and GI cancers comprise a large number of cancers. Applicants have provided no guidance or working examples of any methods of treatment for any diseases using these polynucleotides, or any data or treatment regimen, including even *in vitro* data. Though even *in vitro* data would not be sufficient since no nexus has been established to human diseases. Furthermore, it is not predictable to one of ordinary skill in the art how to use a pharmaceutical composition and this would require undue experimentation to make and use these compositions for every disease that can be treated by these polynucleotides. Applicants can overcome this rejection by amending the claims to recite "A composition comprising the..."

3. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 1, 3, 5 and 6 remain rejected under 35 USC 112, first paragraph, for the reasons already of record on pages 7-8 of the Office Action dated 1/04/01. Applicants argue that the fragments recited in claim 1 encode polypeptides with at least one biological activity of an OGFr.

This argument has been considered, but is not deemed persuasive for at least the reasons already set forth in the above rejection under 35 USC 101. Since the utility of (human) SEQ ID NO:4, 5, 7, 9, 11 and 13, or the encoded proteins has not been established, then it holds that there is a lack of adequate guidance which fragments would have "at least one biological activity of an OGFr" since Applicants have not identified or described what these critical residues are which would provide the claimed activity, including, for example, binding to Met-enkephalin or inhibiting cell growth.

In addition, Applicants have amended claim 3 to recite hybridization conditions. However, an important step in the procedure, the temperature of the wash step, has been omitted from the claim. Applicants would not be entitled to, for example, all nucleic acid molecules which hybridize under the conditions recited in claim 3 (which include the low stringency conditions of 2x SSC), but which remain hybridized in a wash temperature of, for example, 40°C since this would be too low. Therefore, Applicants have not demonstrated that they were in possession of the enormous number of nucleic acid molecules which could hybridize to the claimed sequences under a potentially low wash step. *A high temperature wash step (e.g. 65°C) ,**without adding new matter,** would withdraw the rejection of claim 3 and its dependent claims, 5, 6, 14, 16 and 17 with regard to SEQ ID NO:1 only. However, since SEQ ID NO:4, 5, 7, 9, 11 and 13 have not been shown to have utility, then Applicants have not taught the artisan how to use nucleic acid molecules which hybridize to these sequences.*

4. Claim Rejections - 35 USC § 112, second paragraph

A. Claims 3, 5, 6, 16 and 17 remain rejected under 35 USC 112, second paragraph, for the reasons already of record on page 8 of the Office Action dated 1/4/01. Applicants have amended claim 3 to recite some hybridization parameters. However, the wide range and low stringency of the conditions (.1 – 2x SSC) and the lack of the important wash temperature still make this claim, and the dependent claims indefinite.

5. Claim Rejections - 35 USC § 102

A. Claims 1, 5, 6, 14, 16 and 17 remain rejected under 35 USC 102(b) as being anticipated by Bonaldo et al. (Sequence Comparison A) for the reasons already of record on page 9 of the Office Action dated 1/4/01. Applicants argue that the reference is not anticipated by the amended claims since they recite hybridization conditions and that the protein has a biological activity of an OGFr. However, the polypeptide of Bonaldo et al. has a 97.5% local similarity to SEQ ID NO:1 with numerous areas of 100% identity throughout 70-80 nucleotides. Due to the extremely high overlap between the molecule of Bonaldo et al. and SEQ ID NO:1 of the present invention, the molecule (fragment) of Bonaldo et al. would be expected to hybridize under the conditions given regardless of the temperature of the wash step, if provided. Applicants also argue that the protein of Bonaldo et al. does not recite a biological activity of an OGFr. However, no biological activity of an OGFr has been provided in the claims and the specification only provides activity by example. Therefore, taken its broadest reasonable interpretation, the protein of Bonaldo et al. would be expected to interact with water molecules as a biological activity since proteins are in solution whether inside a cell or secreted. The vector as recited in claim 5 is also taught as seen in Figures 3 and 4. One of ordinary skill in the art would immediately envision the nucleic acid and vectors in a pharmaceutically acceptable carrier, such as water or buffer.

B. Claims 1, 5, 6, 14, 16 and 17 remain rejected under 35 USC 102(b) as being anticipated by Pellett et al. (Sequence Comparisons B-E) for the reasons already of record on page 10 of the Office Action dated 1/4/01. Applicants argue that the reference is not anticipated by the amended claims since they recite that the protein has a biological activity of an OGFr. However, no biological activity of an OGFr has been provided in the claims and the specification only provides activity by example. Therefore, taken its broadest reasonable interpretation, the protein of Pellett et al. would be expected to interact with water molecules as a biological activity since proteins are in solution whether inside a cell or secreted. The vector as recited in claim 5 is, therefore, also taught by Pellett et al. One of ordinary skill in the art would immediately envision the nucleic acid and vectors in a pharmaceutically acceptable carrier, such as water or buffer.

In anticipation of an argument by Applicants, the polypeptide of Pellett et al. has regions of 7-8 nucleotide overlaps with SEQ ID NO:1. Since the *range* of hybridization conditions recited in the claims include that of low salt, and no wash temperature is provided, the molecules (fragment) of Pellett et al. would be expected to hybridize under the conditions given.

C. Claims 1, 5, 14 and 16 remain rejected under 35 USC 102(b) as being anticipated by Fliegel et al. (Sequence Comparison F) for the reasons already of record on page 10 of the Office Action dated 1/4/01. Applicants argue that the reference is not anticipated by the amended claims since they recite that the protein has a biological activity of an OGFr. However, no biological activity of an OGFr has been provided in the claims and the specification only provides activity by example. Therefore, taken its broadest reasonable interpretation, the protein of Fliegel et al. would be expected to interact with water molecules as a biological activity since proteins are in solution whether inside a cell or secreted. The vector as recited in claim 5 is, therefore, also taught by Fliegel et al. One of ordinary skill in the art would

immediately envision the nucleic acid and vectors in a pharmaceutically acceptable carrier, such as water or buffer.

In anticipation of an argument by Applicants, the polypeptide of Fliegel et al. has numerous regions of 7 nucleotide overlaps with SEQ ID NO:1. Since the *range* of hybridization conditions recited in the claims include that of low salt, and no wash temperature is provided, the molecules (fragment) of Fliegel et al. would be expected to hybridize under the conditions given.

D. Claims 1, 5, 14 and 16 remain rejected under 35 USC 102(b) as being anticipated by Everett et al. (Sequence Comparison G) for the reasons already of record on pages 10-11 of the Office Action dated 1/4/01. Applicants argue that the reference is not anticipated by the amended claims since they recite that the protein has a biological activity of an OGFr. However, no biological activity of an OGFr has been provided in the claims and the specification only provides activity by example. Therefore, taken its broadest reasonable interpretation, the protein of Everett et al. would be expected to interact with water molecules as a biological activity since proteins are in solution whether inside a cell or secreted. The vector as recited in claim 5 is, therefore, also taught by Everett et al. One of ordinary skill in the art would immediately envision the nucleic acid and vectors in a pharmaceutically acceptable carrier, such as water or buffer.

In anticipation of an argument by Applicants, the polypeptide of Everett et al. has regions of 7-8 nucleotide overlaps with SEQ ID NO:1. Since the *range* of hybridization conditions recited in the claims include that of low salt, and no wash temperature is provided, the molecules (fragment) of Everett et al. would be expected to hybridize under the conditions given.

E. Claims 1, 5, 6, 14, 16 and 17 remain rejected under 35 USC 102(e) as being anticipated by Chambon et al. (Sequence Comparison H-J) for the reasons already of record on page 11 of the Office Action dated 1/4/01. Applicants argue that the reference is not anticipated by the amended claims since they recite that the protein has a biological activity of an OGFr. However, no biological activity of an OGFr has been provided in the claims and the specification only provides activity by example. Therefore, taken its broadest reasonable interpretation, the protein of Chambon et al. would be expected to interact with water molecules as a biological activity since proteins are in solution whether inside a cell or secreted. The vector as recited in claim 5 is, therefore, also taught by Chambon et al. One of ordinary skill in the art would immediately envision the nucleic acid and vectors in a pharmaceutically acceptable carrier, such as water or buffer.

In anticipation of an argument by Applicants, the polypeptide of Chambon et al. has regions of 7-8 nucleotide overlaps with SEQ ID NO:1. Since the *range* of hybridization conditions recited in the claims include that of low salt, and no wash temperature is provided, the molecules (fragment) of Chambon et al. would be expected to hybridize under the conditions given.

6. Claim Rejections - 35 USC § 103

E. Claim 6 remains rejected under 35 USC 103(a) as being unpatentable over the primary references, Bonaldo et al., Fliegel et al. and Everett et al., each in view of Chambon et al. for the reasons already of record on pages 11-12 of the Office Action dated 1/4/01. Applicants argue that the primary references are not anticipated by the amended claims since they recite that the protein has a biological activity of an OGFr. However, no biological activity of an OGFr has been provided in the claims and the specification only provides activity by example. Therefore, taken its broadest reasonable interpretation, the proteins of each of the primary references would be expected to interact with water molecules as a biological activity since proteins are in solution whether inside a cell or secreted. The vector as recited in

claim 5 is, therefore, also taught by Chambon et al. One of ordinary skill in the art would immediately envision the nucleic acid and vectors in a pharmaceutically acceptable carrier, such as water or buffer.

In anticipation of an argument by Applicants, the polypeptides of the three primary references have numerous regions of at least 7-8 nucleotide overlaps with SEQ ID NO:1. Since the *range* of hybridization conditions recited in the claims include that of low salt, and no wash temperature is provided, the molecules (fragment) of the primary references would be expected to hybridize under the conditions given.

New Claim Objections

A. The syntax of claim 38 could be improved by replacing the phrase "a sequence" with "the sequence."

New Claim Rejections

1. Claim Rejections - 35 USC § 112, first paragraph – written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claim 39 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a genus claim. Nucleic acid molecules which are "**at least 75% identical**" to the proteins of SEQ ID NO:2, 6, 8, 10, 12 or 14 would encode for a protein with one or more amino acid substitutions, deletions, insertions and/or additions to the protein encoded for by SEQ ID NO:2, 6, 8, 10, 12 and 14.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although these types of changes are routinely done in the art, the specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the nucleic acid or protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:2, 5 and 32, or molecules which hybridize to the polynucleotides encoding these SEQ ID NOs (which could be at least thousands of molecules) alone are insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

Applicants could overcome this rejection regarding "75%" by amending the claim to recite that the claimed isolated nucleic acids of claim 39 encode a protein which is at least "95%" identical to the proteins of SEQ ID NO:2, 6, 8, 10, 12 and 14 and in which the protein has a *specific* function, **without adding new matter.**

2. Claim Rejections - 35 USC § 112, first paragraph - enablement

A. Claim 39 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to claiming all nucleic acid molecules which encode proteins which are **"at least 75% identical"** to SEQ ID NO:2, 6, 8, 10, 12 and 14. Nucleic acid molecules which encode proteins which are "at least 75% identical" to the proteins of SEQ ID NO:2, 6, 8, 10, 12 and 14 would encode for a protein with one or more amino acid substitutions, deletions, insertions and/or additions to the protein encoded for by these SEQ ID NOs.

Applicants provide no guidance or working examples of nucleic acid molecules which hybridize to SEQ ID NO:2, 5 or 32, nor do they provide a *function* of these nucleic acid molecules, or of the proteins which they encode. Furthermore, it is not predictable to one of ordinary skill in the art what the functions of these nucleic acids, or the proteins which they encode, are.

Since the utility of SEQ ID NO:4, 5, 7, 9, 11 and 13, or the encoded proteins has not been established as discussed in the above rejection under 35 USC 101, then it is not apparent to one of ordinary skill in the art how to use these proteins which are at least 75% identical since these proteins would also have no utility. Furthermore, Applicants have not required that the proteins encoded for by the nucleic acid molecules of the invention have any specific activities Therefore, Applicants would not be entitled to the breadth of these claims. Applicants have not enabled the artisan what nucleotides or amino acid residues are critical to perform the functions of the proteins encoded for by the claimed polynucleotides.

In summary, the breadth of the claims is extensive with regard to Applicants claiming all nucleic acids which encode proteins which are at least 75% identical to SEQ ID NO:2, 6, 8, 10, 12 and 14. There is also a lack of guidance and working examples of these nucleic acid molecules. Applicants do not

provide a function of these nucleic acid molecules, or a function of the proteins which they encode. These factors, along with the lack of predictability to one of ordinary skill in the art as to what the functions of these nucleic acids are, or the proteins which they encode are, as well as what residues are critical for receptor function, leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

3. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 5, 6, 14, 16, 17 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 3 and 9 are confusing since "complement" can refer to a little as one nucleotide. It is suggested that the claims be amended to recite "full-length complement."

4. Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

A. Claim 39 rejected under 35 U.S.C. 103(a) as being unpatentable over Geisel et al. (Sequence Comaprison A1) in view of Sibson et al. (WO 94/01548). The claim recites an isolated nucleic acid

encoding an OGFr protein which is at least 75% identical to SEQ ID NO:2. The nucleic acid of Geisel et al. encodes a protein which is 95.7% identical to SEQ ID NO:2. Geisel et al. do not teach that this nucleic acid encodes a protein. However, Sibson et al. do teach that it would be desirable to produce proteins from ESTs (pages 8-13).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the invention of Sibson et al. by substituting a cDNA in the polycloning region of the vector with the polynucleotide (cDNA) of Geisel et al. for the purpose of transfecting a host cell as taught by Sibson et al. in view of Sibson et al.'s suggestion that it would be desirable to do so (pages 8-13). One of ordinary skill in the art would have been motivated to make this substitution in order to express the protein encoded by the introduced DNA in a host cell to perform ligand binding and functional assays. There would have been a reasonable expectation of success for a person of ordinary skill in the art to make this invention since these techniques are widely used in the art and are highly successful (Sibson et al., page 10, line 38 – page 12, line 42). Though Geisel et al. do not teach that their protein is an OGFr, it is inherent that a nucleic acid encoding a protein which is 95.7% identical to SEQ ID NO:2, would encode for an OGFr since the sole structural limitation is that the protein only be at least 75% identical to SEQ ID NO:2. The present invention, therefore, is *prima facia* obvious over the above references in the absence of evidence to the contrary.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
July 13, 2001

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